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Practitioner's Docket No. U 012473-1 *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Number: US 6,780,436 B1
Issued: August 24, 2004
Name of Patentee: López-Cabrera et al
Title of Invention: SOLID ORAL PHARMACEUTICAL FORMULATION OF MODIFIED RELEASE THAT CONTAINS AN ACID LABILE BENZIMIDAZOLE COMPOUND

09/660,022

Certificate of Correction Branch
Director of the United States Patent and Trademark Office
P. O. Box 1450
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Certificate
OCT 21 2004
of Correction

ATTENTION: Certificate of Correction Branch
of the Office of Patent Publication

REQUEST FOR CERTIFICATE OF CORRECTION OF PATENT FOR PTO MISTAKE (37 C.F.R. §1.322(a))

NOTE: "If such a request for correction was incurred through the fault of the United States Patent and Trademark Office (Office), and is clearly disclosed in the records of the Office, and is accompanied by documentation that unequivocally supports the patentee's assertion(s), a Certificate of Correction will be expeditiously issued. Such supporting documentation can consist of relevant photocopied receipts, manuscript pages, correspondence dated and received by the Office, photocopies of Examiners' responses regarding entry of amendments, or any other validation that supports the patentee's request so that the request can be processed without the patent file." Notice of September 17, 2002, 1262 OG 96.

1. Attached is Form PTO—1050 (PTO/SB/44) suitable for printing.

NOTE: Form PTO-1050 (or PTO/SB/44), using the column and line number in the printed patent, should be used exclusively regardless of the length or complexity of the subject matter. M.P.E.P. § 1485, 7th ed.

NOTE: The patent grant should be retained by the patentee. The PTO does not attach the Certificate of Correction to the patentee's copy of the patent. The patent grant will be returned to the patentee if submitted. M.P.E.P. § 1485, 8th ed.

2. The exact page and line number where the errors are shown correctly in the application file are:

NOTE: The exact page and line number where the errors occur in the application file should be identified on the request. However, on form PTO/SB/44, only the column and line number in the printed patent should be used. M.P.E.P. § 1480, 8th Edition.

Amendment After Allowance (37 CFR 1.312) filed on March 16, 2004 and entered according to Response to Rule 312 Communication mailed May 17, 2004. A copy is attached

Date: October 5, 2004

3. **Please send the Certificate to:**

Name: Janet I. Cord

Address: c/o Ladas & Parry LLP
26 West 61st Street
New York, NY 10023

(complete, if applicable)

Signature(s) of patentee(s)

or

Signature of assignee or person authorized to sign on behalf of assignee

(type or print name of assignee)

☒ Assignment recorded on January 23, 2001

Reel 011468
Frame 0554

Janet I. Cord
(type or print name of authorized person signing)

Attorney of Record
Title of authorized person signing

☐ Recordal of assignment attached

☐ Attached is a "STATEMENT UNDER 37 CFR 3.73(b)," establishing the right of the assignee to take action in this case.

NOTE: "A certificate of correction, under 35 U.S.C. 254, may be issued at the request of the patentee or [the patentee's] assignee." 37 C.F.R. § 1.322(a). The certificate of correction can be signed by the attorney of record who acts on behalf of the inventor(s) or assignee(s).

PTO/SB/44 (02-01)
Approved for use through 1/31/2004. OMB 0651-0033
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

(Also Form PTO-1050)

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : US 6,780,436 B1
DATED : August 24, 2004
INVENTOR(S): Antonio López-Cabrera
Pedro Juan Solanas-Ibarra
Vincent Mancinelli

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 10, line 59, delete "excipient" insert - - excipients - -

Col. 11, line 3, delete "50:85" insert - - 0.18 to 1:1 (15/85 to 50/50) - -

Col. 11, line 4, delete "5:50"

Col. 11, lines 19-22, delete ", and one or more layers of a mixture of inert, non-alkaline coating, and said system of modified release that comprises an inert, non-alkaline polymer-soluble in water and an inert polymer insoluble in water"

Col. 11, line 27, insert - - of - - between "modified" and "release"

Col. 12, line 40, delete " 50:85 to 15:50" insert - - 0.18 to 1:1 (15/85 to 50/50), - -

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PATENT NO. US 6,780,436 B1

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/660,022	09/12/2000	Antonio Lopez Cabrera	U-012473-1	5837

7590 05/17/2004

Janet I Cord
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New York, NY 10023

EXAMINER	
TRAN, SUSAN T	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 05/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Response to Rule 312 Communication	Application No.	Applicant(s)	
	09/660,022	CABRERA ET AL.	
	Examiner	Art Unit	
	Susan T. Tran	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

1. ☒ The amendment filed on *03/16/04* under 37 CFR 1.312 has been considered, and has been:

   a) ☒ entered.

   b) ☐ entered as directed to matters of form not affecting the scope of the invention.

   c) ☐ disapproved because the amendment was filed after the payment of the issue fee.
   Any amendment filed after the date the issue fee is paid must be accompanied by a petition under 37 CFR 1.313(c)(1) and the required fee to withdraw the application from issue.

   d) ☐ disapproved. See explanation below.

   e) ☐ entered in part. See explanation below.

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Antonio LOPEZ-CABRERA

Serial No.: 09/660,022 Group No.: 1615

Filed: September 12, 2000 Examiner.: Tran, Susan T.

For: SOLID ORAL PHARMACEUTICAL FORMULATION OF MODIFIED RELEASE THAT CONTAINS AN ACID LABILE BENZIMIDAZOLE COMPOUND

Attorney Docket No.: U 012473-1

Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AFTER ALLOWANCE

Reconsideration and further examination is respectfully requested in view of the following amendments and remarks.

In the Claims

1. (Cancelled)

2. (Previously Presented) A pellet according to claim 25 wherein said one or more intermediate layers (c) comprise one or more layers of an inert, non-alkaline coating and one or more layers of a system of modified release.

CERTIFICATE OF MAILING /TRANSMISSION(37 CFR 1.8a)

I hereby certify that this correspondence is, on the date shown below, being:

MAILING

☐ deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to the Assistant Commissioner for Patents, P. O. Box 1450, Alexandria, VA 2313-1450

FACSIMILE

☒ transmitted by facsimile to the Patent and Trademark Office to fax number (703) 872-9306

703-305-4372

Signature

Date: March 16, 2004

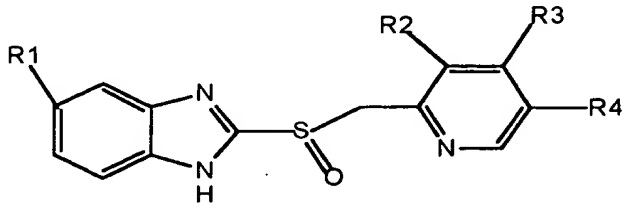
Janet I. Cord
(type or print name of person certifying)

3. (Previously Presented) A pellet according to claim 25 wherein the inert, non-alkaline coating and the system of modified release are mixed in a single layer.

4. (Currently amended) A pellet according to claim 25, in which said one or more intermediate layers (c) comprise a mixture of one or more layers of inert, non-alkaline coating, and one or more layers of said system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water~~, and one or more layers of a mixture of inert, non-alkaline coating, and said system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water~~.

5. (Previously presented) A pellet according to claim 25, wherein the inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients is disposed over the layer (b), wherein the layer comprises the system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water which is disposed over the layer of the inert, non-alkaline coating; and the layer (d) is disposed over the layer formed by the system of modified release comprising an inert non-alkaline polymer soluble in water and an inert polymer insoluble in water.

6. (Previously Presented) A pellet according to claim 25 wherein said acid labile benzimidazole compound is a compound of formula (I)



(I)

wherein

R^1 is hydrogen methoxy or difluoromethoxy;

R^2 is methyl or methoxy;

R^3 is methoxy, 2,2,2-trifluoroethoxy or 3-methoxypropoxy; and

R^4 is hydrogen or methyl.

7. (Previously Presented) A pellet according to claim 25 wherein said acid labile benzimidazole compound is selected from the group consisting of omeprazole, lansoprazole, pantoprazole and mixtures thereof.

8. (Previously Presented) A pellet according to claim 25 wherein said inert, non-alkaline polymer soluble in water, present in the layer (b) is selected from hydroxypropylmethylcellulose (HPMC) and hydroxypropylcellulose (HPC).

9. (Previously Presented) A pellet according to claim 25, wherein said inert, non-alkaline polymer soluble in water of the inert, non-alkaline coating, present in the intermediate layer(s) (c) is hydroxypropylmethylcellulose (HPMC).

10. (Previously Presented) A pellet according to claim 25 wherein said inert, non-alkaline polymer soluble in water of the system of modified release, present in the one or more intermediate layers (c) is hydroxypropylmethylcellulose (HPMC).

11. (Previously Presented) A pellet according to claim 25 wherein said inert polymer insoluble in water of the system of modified release, present in the one or more intermediate layers (c) is ethylcellulose or a copolymer of ammonium methacrylate.

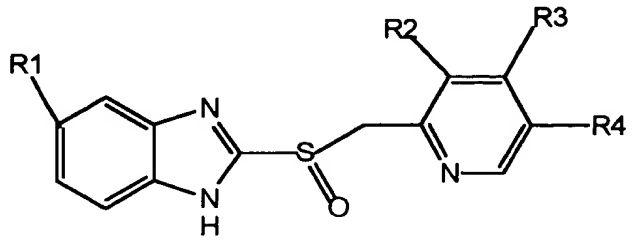
12. (Previously Presented) A pellet according to claim 25 wherein said external layer (d) comprises a gastro-resistant polymer, a plasticizer and one or more pharmaceutically acceptable inert excipients.

13. (Currently amended) A method for obtaining a gastro-resistant pellet of modified release that contains as an active ingredient an acid labile benzimidazole compound, that comprises:
(i)applying an aqueous suspension of an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water, and one or more pharmaceutically acceptable inert excipients to cover an inert nucleus, wherein said inert excipients do not react in the conditions used;

(ii) applying one or more intermediate layers, separated or mixed among themselves that contain (i) an inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients; and (ii) a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water, wherein the weight ratio of the inert, non-alkaline polymer soluble in water to the inert polymer insoluble in water is ~~50:85 to 15:50~~ 0.18 to 1:1 (15/85 to 50/50) ~~to~~ , a plasticizer and an anti-tack agent, separate or mixed; and

(iii) covering said intermediate layer or layers with an aqueous suspension that comprises a gastro-resistant polymer, a plasticizer and one or more pharmaceutically acceptable inert excipients to create an external layer of enteric coating.

14. (Previously Presented) A method according to claim 13 wherein said acid labile benzimidazole compound is a compound of formula (I)



(I)

wherein

R^1 is hydrogen, methoxy or difluoromethoxy;

R^2 is methyl or methoxy;

R^3 is methoxy, 2,2,2-trifluoroethoxy or 3-methoxypropoxy; and

R^4 is hydrogen or methyl.

15. (Previously Presented) A method according to claim 13 wherein said acid labile benzimidazole compound is selected from the group consisting of omeprazole, lansoprazole, pantoprazole and mixtures thereof.

16. (Previously Presented) A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, present in the suspension applied in

step (i) is selected from hydroxypropyl-methylcellulose (HPMC) and hydroxypropylcellulose (HPC).

17. (Previously Presented) A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, comprised in the inert, non-alkaline coating, present in the suspension applied in step (ii) is hydroxypropylmethylcellulose (HPMC).

18. (Previously Presented) A method according to claim 13, wherein, said inert, non-alkaline polymer soluble in water, comprised in the system of modified release, present in the suspension applied in step (ii) is hydroxypropylmethylcellulose (HPMC).

19. (Previously Presented) A method according to claim 13 wherein said inert polymer insoluble in water, comprised in the system of modified release, present in the suspension applied in step (ii) is ethylcellulose or a copolymer of ammonium methacrylate.

20. (Previously Presented) A composition of modified release that comprises one or more pellets of claim 25.

21. (Previously Presented) A composition of modified release comprising a mixture of the pellets of claim 25 having the same release profile.

22. (Previously Presented) A composition of modified release comprising a mixture of the pellets of claim 25 having a different release profile.

23. (Previously Presented) A composition of modified release comprising a mixture of the pellets of claim 25 which have (i) a quick release profile and (ii) a slow release profile in a ratio between 10:90 and 90:10 by weight.

24. (Previously Presented) A composition according to claim 20, in the form of a capsule or a tablet.

25. (Currently amended) A pellet comprising an acid labile benzimidazole compound, wherein the pellet comprises:

(a) an inert nucleus;

(b) a layer disposed over said inert nucleus (a), consisting of an acid labile benzimidazole compound, an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients wherein said excipients do not react in the conditions used;

(c) one or more intermediate layers that comprise:

(i) an inert, non-alkaline coating, formed of an inert, non-alkaline polymer soluble in water and one or more pharmaceutically acceptable inert excipients; and

(ii) a system of modified release that comprises an inert, non-alkaline polymer soluble in water and an inert polymer insoluble in water, wherein the weight ratio of the inert, non-alkaline polymer soluble in water to the inert polymer insoluble in water is ~~50:85 to 15:50~~ 0.18 to 1:1 (15/85 to 50/50) ; said intermediate layer(s) (c) disposed over said layer (b) that covers the inert nucleus; and

(d) an external layer comprising an enteric coating disposed over said intermediate layer(s) (c).

REMARKS

Claims 2-25 are in this application. Claims 4, 13 and 25 have been amended. Claim 4 has been amended to delete text which is a duplicate of text which appears earlier in the claim.

As stated in the Examiner's Amendment which accompanies the Notice of Allowability, Claims 13 and 25 were amended to include **"wherein the weight ratio of the inert, non-alkaline polymer soluble in water (HPMC) to the inert polymer insoluble in water (EC) is 50:85 to 15:50".**

It appears that a mistake has been made when choosing the values of the examples.

The examples of the text of the application are:

HPMC/EC: 45/55, 30/70, 50/50, 40/60, 30/70, 15/85 and 33/67; that is: 0.81, 0.42, 1.00, 0.60, 0.42, 0.18 and 0.44.

This values can be listed in a different order: 1.00, 0.81, 0.60, 0.44, 0.42, 0.42, 0.18.

It appears that the values chosen are the highest values of HPMC and EC: 50 and 85, as well as the lowest values: 15 and 50, to build up the ratio range 50:85 to 15:50, that is, 0.58 to 0.30. However, the ratio range should have been build up choosing also the highest values of HPMC and EC: 50 and 85, as well as the lowest values: 15 and 50, but in a different order (the correct one), so that the range 50/50 to 15/85, that is, 1 to 0.18.

Applicants believe that this is the proper way to define the range since the ratio range 50/50 to 15/85 is fully supported by the examples (example 3 and example 6 of the application). Whereas the ratio range included in the allowed claims is not supported by any of the examples of the patent application. Moreover, since the application as originally filed discloses that "*varying the amount of insoluble polymer with respect to the soluble polymer gives a greater or lesser retarding effect, in general, increasing the amount of insoluble polymer with respect to the amount of soluble polymer leads to a slower release of the active ingredient*", it is strongly believed that the combination of this teaching with the content of the examples would allow the applicant to obtain protection for the

widest ranges covered by the examples.

This amendment is needed to provide the proper protection of the invention. The proposed amended claims require no additional search or examination and are patentable because the weight ratio of polymer soluble in water to polymer insoluble in water is fully supported by the examples and according to notice of allowance, the claims are patentable because of the incorporation of the definition of the inert excipients and incorporation of weight ratio of polymer soluble in water to polymer insoluble in water. Patentability of the claims does not depend on the specific weight ratio of 50:85 to 15:50. The amended claims were not earlier presented because it was on review of the reasons for allowance that the need for the amended claims was recognized.

It is respectfully requested that claims 4, 13 and 25 be amended as proposed.

The Examiner is respectfully requested to contact the undersigned if she has any comments or questions.

Respectfully submitted,

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